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| 09/741,106 | 12/21/2000 | Michael A. Innis | 12441.00003 | 7590 |

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| EXAMINER |
|---|
| KAM, CHIH MIN |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1653 | 7 |

DATE MAILED: 08/13/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. 09/741,106 | Applicant(s) INNIS ET AL. | |
|---|---|---|---|
| | Examiner Chih-Min Kam | Art Unit 1653 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) 1-87 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 1-87 are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

### *Election/Restrictions*

1. Restriction to one of the following inventions is required under 35 U. S. C. 121:

I. Claims 1-27 and 73, drawn to a chimeric protein comprising a Kunitz-type domain 1 of TFPI-2 or TFPI, and a Kunitz-type domain 2 of TFPI or TFPI-2; or a pharmaceutical composition comprising the chimeric protein and a carrier, classified in class 435, subclass 69.7.

II. Claims 28-30 and 74, drawn to a TFPI mutein or a pharmaceutical composition comprising the TFPI mutein and a carrier, classified in class 530, subclass 350.

III. Claims 31-33 and 75, drawn to a TFPI-2 mutein or a pharmaceutical composition comprising the TFPI-2 mutein and a carrier, classified in class 530, subclass 324.

IV. Claims 34, 37, 40 and 43-52, drawn to a nucleic acid encoding the chimeric protein; an expression vector comprising the nucleic acid; a transformed host cell capable of producing the chimeric protein; and a method of producing the chimeric protein by expression of the nucleic acid sequence, classified in class 536, subclass 23.1, and class 435, subclasses 320.1 and 325.

V. Claims 35, 38, 41 and 53-62, drawn to a nucleic acid encoding the TFPI mutein; an expression vector comprising the nucleic acid; a transformed host cell capable of producing the TFPI mutein; and a method of producing the TFPI mutein by expression of the nucleic acid sequence, classified in class 536, subclass 23.1, and class 435, subclasses 320.1 and 325.

VI. Claims 36, 39, 42 and 63-72, drawn to a nucleic acid encoding the TFPI-2 mutein; an expression vector comprising the nucleic acid; a transformed host cell capable of producing the TFPI-2 mutein; and a method of producing the TFPI-2 mutein by expression of the nucleic acid sequence, classified in class 536, subclass 23.1, and class 435, subclasses 320.1 and 325.

VII. Claims 76-78, drawn to a method of treating septic shock, comprising administering the pharmaceutical composition of TFPI-2 protein, classified in class 530, subclass 324.

VIII. Claims 79-81, drawn to a method of treating thrombosis disorders, comprising administering the pharmaceutical composition of TFPI-2 protein, classified in class 530, subclass 324.

IX. Claims 82 and 83, drawn to monoclonal antibody capable of selectively binding to the chimeric protein, classified in class 424, subclass 130.1.

X. Claims 84 and 85, drawn to monoclonal antibody capable of selectively binding to the TFPI mutein, classified in class 424, subclass 130.1.

XI. Claims 86 and 87, drawn to monoclonal antibody capable of selectively binding to the TFPI-2 mutein, classified in class 424, subclass 130.1.

Should Invention I be elected, applicant is required to select one protein for heparin-binding domain from claims 8 and 22; one amino acid sequence for heparin-binding domain from claims 9 and 23; and one amino acid sequence for the second amino acid sequence from claim 15. Each protein or amino acid sequence, absent factual data to the contrary, is a distinct peptide. This is not species election.

2. The inventions are distinct, each from the other because of the following reasons:

Inventions I, II and III are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are drawn to a chimeric protein comprising a Kunitz-type domain 1 of TFPI-2 or TFPI and a Kunitz-type domain 2 of TFPI or TFPI-2; a TFPI mutein; and a TFPI-2 mutein that would have different amino acid sequences, exhibit different chemical properties and produce different effects.

Inventions IV, V and VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are drawn to different nucleic acids, which have different nucleotide sequences and exhibit different functions, e.g., encoding a chimeric protein, a TFPI mutein and a TFPI-2 mutein, respectively.

Inventions IX, X and XI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are drawn to different antibodies, which bind to different proteins, e.g., the chimeric protein, the TFPI mutein and the TFPI-2 mutein.

The polynucleotides of Invention IV are related to the proteins of Invention I because the polynucleotides encode the claimed proteins. The inventions are distinct because they are physically and functionally distinct chemical entities, and the protein products can be made by

another and materially different process, such as chemical peptide synthesis. Further, the polynucleotides may be used for process other than the production of the proteins, such as nucleotide hybridization assay.

The method of Invention IV and the protein of Invention I are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case the proteins as claimed can be made by chemical peptide synthesis.

The protein of Invention I is related to the antibody of Invention IX by virtue of being the cognate antigen, necessary for the production of the antibody. The inventions are distinct because they are physically and functionally distinct chemical entities and because the protein can be used in another and materially different process from the use for production of the antibody such as inhibiting blood coagulation enzymes.

The products of Inventions I, V, VI, X and XI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are drawn to a chimeric protein (Invention I), a nucleic acid (Inventions V and VI) and an antibody (Inventions X and XI), which are patentably distinct each from the other because they are physically and functionally distinct chemical entities and also have different utilities. For example, the protein of Invention I is used for inhibiting coagulation enzymes, while nucleic acids of Inventions V and VI are used for making the TFPI

mutein and TFPI-2 mutein, respectively, and the antibodies of Inventions X and XI specifically bind TFPI mutein and TFPI-2 mutein, and can be used for western blotting.

The product of Invention I is distinct from the methods of Inventions V, VI, VII and VIII because the product of Invention I can neither be made by nor used in the methods of Inventions V, VI, VII and VIII.

The polynucleotides of Invention V are related to the proteins of Invention II because the polynucleotides encode the claimed proteins. The inventions are distinct because they are physically and functionally distinct chemical entities, and the protein products can be made by another and materially different process, such as synthetic peptide synthesis. Further, the polynucleotides may be used for process other than the production of the proteins, such as nucleotide hybridization assay.

The method of Invention V and the protein of Invention II are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case the proteins as claimed can be made by chemical peptide synthesis.

The protein of Invention II is related to the antibody of Invention X by virtue of being the cognate antigen, necessary for the production of the antibody. The inventions are distinct because they are physically and functionally distinct chemical entities and because the protein can be used in another and materially different process from the use for production of the antibody such as inhibiting blood coagulation enzymes.

The products of Inventions II, IV, VI, IX and XI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are drawn to TFPI mutein (Invention II), a nucleic acid (Inventions IV and VI) and an antibody (Inventions IX and XI), which are patentably distinct each from the other because they are physically and functionally distinct chemical entities and also have different utilities. For example, the protein of Invention II is used for inhibiting coagulation enzymes, while nucleic acids of Inventions IV and VI are used for making the chimeric protein and TFPI-2 mutein, respectively, and the antibodies of Inventions IX and XI specifically bind the chimeric protein and TFPI-2 mutein, and can be used for western blotting.

The product of Invention II is distinct from the methods of Inventions IV, VI, VII and VIII because the product of Invention II can neither be made by nor used in the methods of Inventions V, VI, VII and VIII.

The polynucleotides of Invention VI are related to the peptides of Invention III because the polynucleotides encode the claimed peptides. The inventions are distinct because they are physically and functionally distinct chemical entities, and the protein products can be made by another and materially different process, such as synthetic peptide synthesis. Further, the polynucleotides may be used for process other than the production of the proteins, such as nucleotide hybridization assay.

The method of Invention VI and the protein of Invention III are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product

or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case the proteins as claimed can be made by chemical peptide synthesis.

The product of Invention III and the methods of Inventions VII and VIII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the methods of Inventions VII and VIII are alternative processes of use of the product of Invention III.

The protein of Invention III is related to the antibody of Invention XI by virtue of being the cognate antigen, necessary for the production of the antibody. The inventions are distinct because they are physically and functionally distinct chemical entities and because the protein can be used in another and materially different process from the use for production of the antibody such as inhibiting blood coagulation enzymes.

The products of Inventions III, IV, V, IX and X are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are drawn to TFPI-2 mutein (Invention III), a nucleic acid (Inventions IV and V) and an antibody (Inventions IX and X), which are patentably distinct each from the other because they are physically and functionally distinct chemical entities and also have different utilities. For example, the protein of Invention III is used for inhibiting coagulation enzymes, while nucleic acids of Inventions IV and V are used for making the

chimeric protein and TFPI mutein, respectively, and the antibodies of Inventions IX and X specifically bind the chimeric protein and TFPI mutein, and can be used for western blotting.

The product of Invention III is distinct from the methods of Inventions IV and V because the product of Invention III can neither be made by nor used in the methods of Inventions IV and V.

The methods of Inventions IV-VIII are patentably distinct each from the other because they have different method steps, utilize different materials and produce different results.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification and their recognized divergent subject matter, and because each invention requires different searches but are not co-extensive, examination of these distinct inventions would pose a serious burden on the examiner and therefore restriction for examination purposes as indicated is proper.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement is traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (703) 308-9437. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, Ph. D. can be reached on (703) 308-2923. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-0294 for regular communications and (703) 308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Chih-Min Kam, Ph. D. CMK
Patent Examiner

Karen Cochrane Carlson PhD

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER

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August 7, 2002